

Clinical Laboratory Improvement Advisory Committee

Summary Report
May 10-11, 1995



U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service



Clinical Laboratory Improvement Advisory Committee

May 10-11, 1995

Summary

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Record of Attendance

The Clinical Laboratory Improvement Advisory Committee (CLIAC) met at the Centers for Disease Control and Prevention (CDC), Auditorium A, in Atlanta, Georgia, on May 10-11, 1995. Those in attendance are listed below:

Committee Members

Dr. J. Scott Abercrombie
Dr. Paul Bachner
Dr. Regina Benjamin
Ms. Michelle Best
Ms. Virginia Charles
Dr. Susanne Gollin
Dr. Stanley Inhorn
Dr. Verlin Janzen
Ms. Sandra Johnson
Dr. J. Stephen Kroger
Dr. Bereneice Madison
Dr. Kenneth Matthews
Dr. Wendell O'Neal
Dr. Glenda Price
Ms. Deborah Reed
Dr. Patricia Saigo
Dr. Morton Schwartz
Mr. Elliott Segal
Dr. Ulder Tillman

Ex Officio Members

Dr. Carlyn Collins, CDC
Dr. Steve Gutman, FDA
Ms. Judith Yost, HCFA

Executive Secretary

Dr. Edward Baker

Liaison Representatives

Dr. Fred Lasky (HIMA)

Centers for Disease Control and Prevention

Ms. Nancy Anderson	Mr. Edwin Holmes
Ms. Rosemary Bakes-Martin	Dr. Dick Keenlyside
Ms. Louise Barden	Dr. Katherine Kelley
Ms. Carol Bigelow	Dr. John Krolak
Dr. Joe Boone	Dr. John C. Ridderhof
Ms. Sheila Boring	Ms. Eunice Rosner
Ms. Genoria Bridgeman	Dr. Shahram Shahangian
Ms. Cheryl Coble	Ms. Elva Smith
Ms. Debbie Coker	Dr. Steve Steindel
Ms. Carol Cook	Dr. Tina Stull
Ms. Crystal Frazier	Ms. Julie Wasil
Ms. MariBeth Gagnon	Ms. Rhonda Whalen
Ms. Sharon Granade	Mr. Mark White
Mr. Tom Hearn	

Clinical Laboratory Improvement Advisory Committee

The Secretary of Health and Human Services is authorized under Section 353 of the Public Health Service Act, as amended, to establish standards to assure consistent, accurate, and reliable test results by all clinical laboratories in the United States. The Secretary is authorized under Section 222 to establish advisory committees.

The Clinical Laboratory Improvement Advisory Committee (CLIAC) was chartered in February 1992 to provide scientific and technical advice and guidance to the Secretary and the Assistant Secretary for Health regarding the need for, and the nature of, revisions to the standards under which clinical laboratories are regulated; the impact on medical and laboratory practice of proposed revisions to the standards; and the modification of the standards to accommodate technological advances.

The Committee consists of 20 members, including the Chair. Members are selected by the Secretary from authorities knowledgeable in the fields of microbiology, immunology, chemistry, hematology, pathology, and representatives of medical technology, public health, clinical practice, and consumers. In addition, CLIAC includes three ex officio members, or designees: the Director, Centers for Disease Control and Prevention; the Commissioner, Food and Drug Administration; and the Administrator, Health Care Financing Administration; and such additional officers of the U.S. Government that the Secretary deems are necessary for the Committee to effectively carry out its functions. CLIAC will also include a non-voting liaison representative who is a member of the Health Industry Manufacturers Association and such other non-voting liaison representatives that the Secretary deems are necessary for the Committee to effectively carry out its functions.

Due to the diversity of its membership, CLIAC is at times divided in the guidance and advice it offers to the Secretary. Even when all CLIAC members agree on a specific recommendation, the Secretary may not follow their advice due to other overriding concerns. Thus, while some of the actions recommended by CLIAC may eventually result in changes to the law, the reader should not infer that all of the advisory committee's recommendations will be automatically accepted and acted upon by the Secretary.

Welcome and Announcements

The meeting was called to order by Dr. Morton Schwartz, Clinical Laboratory Improvement Advisory Committee (CLIAC) Chairman who welcomed the Committee members. Self-introductions were made by all members of CLIAC, and Dr. Schwartz stated the role and function of the CLIAC. Dr. Edward Baker, Director of the Public Health Practice Program Office, Centers for Disease Control and Prevention (CDC), and Executive Secretary of CLIAC, made additional welcoming remarks and announcements. Mr. Kevin Malone, Attorney Advisor, CDC, reviewed the conflict of interest forms and format for disclosure of each committee member's relevant financial interests as they relate to any topics discussed during the CLIAC meeting.

Presentations and Committee Discussion

CLIA UPDATE/CDC

CLIA Regulations/Archer Bill

Addendum A

Dr. Carlyn Collins, Director of the Division of Laboratory Systems (DLS), presented a status report on the Clinical Laboratory Improvement Amendments (CLIA) regulations. Dr. Collins explained that revisions to the CLIA regulations pertaining to the moderate complexity subcategory, physician-performed microscopy, and qualification requirements for general supervisor and high complexity testing personnel were published as a final rule with comment in the Federal Register on April 24, 1995. She further explained that the proposed rule to clarify the waived criteria and the proposed rule to solicit comments on a new subcategory of moderate complexity, accurate and precise technology (APT) tests, are currently under Department review. Dr. Collins also briefly reviewed the Archer bill (H.R. 1386 and introduced in the Senate as S.877). Dr. Collins explained that the Archer bill would amend the CLIA law to exempt physician office laboratories (POLs) in which tests are performed as an adjunct to other services. POLs that perform pap smears would not be exempt. In the bill, "physician" is defined by reference to the Social Security Act which includes a Doctor of Medicine or Osteopathy, a Doctor of Dental Surgery or of Dental Medicine, a Doctor of Podiatric Medicine, and a Doctor of Optometry. Copies of the Archer bill were provided to the committee members.

Committee Discussion

Members questioned whether the revisions to the CLIA regulations published April 24, 1995 contained the same language as the CLIAC recommendations for changes to the CLIA requirements. Explanation was given by CDC that the language in the April 24, 1995 regulation was the same as the Committee recommendations with the addition of dates pertinent to the personnel sections. A committee member asked if the CLIAC recommendations that were not

included in the CLIA rule published April 24, 1995 would be in the final regulation. Dr. Collins responded that there were still a number of important areas to be addressed in the final, final regulation. A committee member requested a list of the CLIAC recommendations and their current status. This was provided to the committee members by CDC. **(See Addendum B)**

A committee member questioned why the Department would proceed to develop regulations for APT categorization when the CLIAC had expressed reservations about the subcategory. Dr. Collins explained that although there were previous discussions with the CLIAC on APT, Committee input was not the only factor considered. Because of broad public interest, the APT regulation has been developed as a proposed rule to allow increased opportunity for public input and solicitation of comments. Dr. Baker pointed out that in previous discussions, CLIAC indicated that the complexity model needed refinement. Publishing APT as a proposed rule would allow the public to submit suggestions for revisions to the subcategory and revisions to improve the complexity model. After the comment period, CDC could analyze the comments and at a future CLIAC meeting, the comments could be summarized for Committee discussion. Dr. Schwartz requested that a Committee meeting be scheduled to discuss the comments to the APT proposed rule before publication of the final rule.

One committee member asked if the Archer bill would exempt POLs that accept referral specimens. Dr. Collins explained that the bill could include POLs that accept referral specimens and pathologists' laboratories, but that, at this time, it was unclear how the bill was to be interpreted.

Review of the CDC Process for Waiving Tests

Addendum C

A review and update of the process for evaluating applications for waiver was presented by Ms. Rosemary Bakes-Martin, Laboratory Practice Standards Branch. Ms. Bakes-Martin explained that the moratorium on adding tests to the waived category was lifted in December. Letters were sent to manufacturers announcing the end of the moratorium and providing guidelines for submitting requests for waiver. The guidelines followed the clarifications to the waived criteria previously discussed and reviewed by CLIAC. In May, manufacturers were notified that test systems cleared by the Food and Drug Administration (FDA) for home use would be waived and were provided additional clarification in some areas of the guidelines. Ms. Bakes-Martin described the process for reviewing waiver submissions, calling it a very interactive process and stated that to date, ten manufacturers have requested waiver on 22 analyte/test system combinations. Two test systems have been granted waiver, Chemtrak Accumeter (also known as Johnson and Johnson Advance Care) total cholesterol and HemoCue glucose. The Chemtrak Accumeter test system was granted waiver based on FDA clearance for home use. The HemoCue glucose test system met the CDC guidelines to the waived criteria and was approved for waiver.

Committee Discussion

Committee members asked a few general questions about the waiver process, and Dr. Schwartz explained that previously the Committee had been involved in reviewing CDC's clarifications to the waiver criteria but had requested not to be routinely involved in reviewing individual test systems that applied for waiver. Dr. Baker outlined the following as possible CLIAC roles: at CDC's request, CLIAC may be asked to review clarifications to the statutory criteria for waiver; provide oversight in the implementation process; and while CLIAC would not be performing individual test system reviews, it may be asked to evaluate application of the guidelines to a specific device.

Most of the members expressed some concern about the criteria used by the FDA for home use clearance and the policy to waive under CLIA, tests cleared by the FDA for home use. Committee members asked whether CDC conducts literature searches since some of the products already cleared for home use have problems that have been well documented in various publications. The Committee also asked whether this waiver review was considered an interim process since the proposed rule to clarify the waived criteria had not been published. The Committee then asked what would happen to those devices receiving waiver during this interim period once the clarifications to the waived criteria are finalized. Ms. Bakes-Martin explained that test systems approved for waiver would be published as a notice in the Federal Register with opportunity for public comment and a test system's waiver status could change based on comment analysis. It was also explained that there could be some revisions to the waiver process, but any revisions to the process would probably not be major, and devices waived during this interim period would probably meet the requirements in the final rule for waiver. Ms. Bakes-Martin added that waiver is effective on the date of notification to the manufacturer. A notification letter is also sent to the Health Care Financing Administration (HCFA). In addition, the test categorization list, which is available on the Internet, is updated monthly.

Another member reiterated that when the Committee had previously discussed the three statutory criteria for waiver, there had been agreement that the decision for waiver would be based on performance and that some devices cleared for home use were poor performers and would not meet the performance criteria. Dr. Collins responded that, in accordance with a CLIAC recommendation, those devices previously waived would be subject to any new criteria when finalized and this provision was included in the proposed rule for test waiver.

The Committee's manufacturer liaison asked if the waiver application was evaluated simultaneously with the FDA review for new products and questioned the CDC's request for raw data when the FDA only requires submission of raw data for clearance of Class III devices. CDC stated that the two review processes are conducted simultaneously, and the manufacturer is notified of the waiver decision once FDA clearance is obtained. CDC also explained that the waiver review is focused on the performance studies and whether the specific waived criteria are met. Many of the waiver requests have only included manufacturer's summary data which has not been sufficient to evaluate the test system performance to verify that the waived criteria are

met. When the manufacturer provided raw data, the CDC was able to do the statistical analysis and determine whether specific performance specifications were met. Ms. Bakes-Martin emphasized that the CDC has been working closely with manufacturers and the waiver review process has been going well. Again, the manufacturer liaison noted that the submission of summary versus raw data was an issue and expressed concern about government resources being used to perform statistical analysis when manufacturers should be doing their own statistical analysis. Another committee member countered that requiring submission of raw data allows CDC to perform the analysis needed and can be used to validate the manufacturers' summary data. One member reiterated that, at a future meeting, it would be useful for the CDC to demonstrate how the guidelines are applied to specific test systems.

Summary of Research Data and Analysis Activities

Addendum D

Dr. Tom Hearn, Chief, Laboratory Practice Assessment Branch, presented some of the CDC CLIA research and data analysis activities and noted that the data came from a variety of sources. Demographic information was presented about the nation's clinical laboratories. Volume and scope of testing information for specific laboratory types was also presented. Information on laboratory practice including personnel data and quality assurance practices followed. The presentation concluded with laboratory performance indicators based on proficiency testing (PT) and inspection data, and a discussion of the numerous factors currently influenced by the practice of clinical laboratory medicine.

It was announced that a clinical laboratory medicine research institute is planned for October of this year entitled, "Frontiers in Laboratory Practice Research." The institute will provide a forum for presentation of existing research and data in the clinical laboratory arena, and will include an open discussion of the current research methods, agendas, and strategic planning for the future of research in clinical laboratory medicine.

Committee Discussion

Several committee members requested clarification of the data pertaining to PT performance. The CLIAC Chairman commented that the number of laboratory closures after the implementation of the CLIA program was remarkably small in comparison to what has been reported by some groups. CDC responded that this data and results of an Office of the Inspector General study did not support the prediction that numerous laboratories would close due to CLIA. However, one committee member noted that the data shows that 20% of POLs have reduced the amount of testing performed. Dr. Hearn responded that a reduction in performance of a few microbiology procedures probably accounted for the majority of the decreases in testing. Dr. Hearn added that other factors may also have contributed to some reductions in testing services. For example, shifts from solo to group practice, and shifts from fee-for-service practices to managed care, practice guidelines, and financial considerations. Another committee member noted the discrepancy between information included in the Regulatory Impact Analysis

in the February 1992 CLIA regulations, which predicted that 15% of all laboratories would be waived, and current HCFA certification data which shows 45% of all laboratories are waived. Ms. Judy Yost reminded the Committee that the estimated number of waived laboratories predicted by the Regulatory Impact Analysis was based on unverified assumptions as no data were available in 1992 to indicate either the number of laboratories in operation or the types of services performed by these laboratories.

One committee member suggested that it would be valuable to have baseline data on the number of unregulated laboratories versus regulated laboratories prior to CLIA implementation, and the number of POLs compared to other laboratory types, to accurately ascertain if CLIA has affected performance. Another committee member pointed out that although the data reflects that a number of laboratories have PT failures, POLs have shown significant improvement in PT performance over time, a finding which is consistent with the data recently published by the College of American Pathologists (CAP). A committee member stated that the inspection data on POLs presents a persuasive argument showing POLs can benefit from and should be subject to regulation. One committee member noted that insurance companies are looking for an objective standard such as laboratory accreditation or certification to serve as a quality indicator of laboratory testing in POLs. Another committee member noted that exempting POLs from CLIA, as proposed in the Archer bill, might not be necessary if the shift from solo or small group practices to managed care continues.

One committee member noted that physicians do not initiate patient care and treatment based solely on laboratory values; other factors such as the physical examination are also considered. The Chairman suggested that when a patient is available for a direct evaluation by the physician, an unexpected laboratory value should not be ignored. Instead, the laboratory value should alert the doctor to reevaluate the patient's condition.

A committee member asked if any studies have been done to determine whether there were improvements in patient outcomes as a result of quality improvements in laboratory testing. Dr. Tina Stull, Laboratory Practice Assessment Branch, stated the CDC has a cooperative agreement with the Ambulatory Sentinel Practice Network to determine the nature and frequency of problems in the total testing process, and their impact on patient care. While the study is not yet completed, early data indicates that most laboratory problems (60%) occur in the initial or pre-analytic phase of testing, while 15% occur in the analytic phase of testing. Dr. Stull commented that, in reality, the percentage of analytic phase problems may be higher but some "analytic-type" errors may not be as apparent to the physician. In response, one committee member commented that in a POL there should be less chance of errors occurring in the pre and postanalytic phases of testing since specimens are generally collected and tested at the time of the patient visit thereby eliminating errors during specimen transport and result reporting.

Overall, the Committee was impressed with the research studies and agreed this type of data is critical for monitoring and evaluating laboratory practices, and the implementation of the CLIA program.

**CLIA UPDATE/HCFA
Summary of HCFA Survey Data**

Addendum E

Ms. Judith Yost, of the HCFA, presented an update on CLIA registration/certification, inspection findings, and enforcement activities. At the completion of the first inspection cycle, 20% of the laboratories had no deficiencies. The most common condition level deficiency was failure to enroll in proficiency testing (59%) and the most common deficiency overall was failure to test two levels of controls. Laboratory enforcement actions taken include the following: 8 certificate limitations; 8 certificate suspensions; 11 certificate revocations; and 14 suspensions of Medicare payments. HCFA continues to employ a consultative, educational approach to inspections to assist laboratories in achieving compliance with the CLIA regulations.

Committee Discussion

A few committee members asked specific questions regarding the CLIA inspection data, such as, were PT deficiencies due to failure to enroll in any PT program or failure to enroll in a PT program for specific regulated analytes and which type of laboratories had no deficiencies? Ms. Yost answered that condition deficiencies in PT included failure to enroll for any regulated analyte for which the laboratory was performing patient testing or significant PT deficiencies; and the breakdown of laboratories with no deficiencies were 17% POL, 25% independent, and 13% hospital. It was noted that preliminary data on second cycle inspections indicate that laboratories continue to show improvement in complying with the CLIA regulations, as evidenced by fewer deficiency citations. Another member stated that the Commission on Office Laboratory Accreditation (COLA) is developing a paper for publication that will discuss whether there is any significant change in laboratory performance over time due to enrollment in an accreditation program. The committee member added that, in general, COLA accredited laboratories inspected during the second inspection cycle were showing significant improvement.

Proposal for a Performance-Based Survey Process

Addendum F

Ms. Yost also presented some general information regarding a proposal to establish a performance-based survey process which would be consistent with the Administration's "reinventing government" efforts to ensure that regulations are appropriate and effective and reduce the regulatory burden when possible. Additionally, it was noted that the total quality management approach provides a rationale for improving the survey process and recognizing and rewarding laboratories that have demonstrated compliance. Ms. Yost commented that this process would be more outcome-oriented and more efficient since on-site surveys would be focused on those laboratories with problems. Good laboratory performers would be recognized and allowed to complete a questionnaire (off-site paper survey) in lieu of an on-site inspection. She then asked the Committee for comments on this approach for improving the survey process.

Committee Discussion

A majority of the Committee expressed strong support and agreement with the suggested approach to improve the existing CLIA inspection process. In particular, the Committee agreed with focusing more on the outcome rather than process and rewarding laboratories that are good performers. Members of the Committee asked the following specific questions: would the laboratory be required to retain records for four years when the inspection cycle shifted from two to four years and would the off-site paper survey be optional for the states or would all states have to participate? Ms. Yost clarified that only one on-site inspection cycle would be skipped and that no changes in the record retention requirements are anticipated; laboratories would continue to maintain records for two years. In addition, any revisions to the process would have to be consistent in all states and surveyors would need orientation training in the new process. Committee members noted that the CAP and COLA accreditation programs have developed questionnaires for off-site evaluation purposes. One member commented that this approach also has been used for years in industry and worked well.

Other committee members suggested consideration be given to those laboratories having only minor deficiencies rather than requiring laboratories to be 100% deficiency-free in order to be eligible for the offsite survey. Also, one member cautioned against evaluating quality assurance practices too rigorously until there are defined standards, while another member noted that care must be taken to ensure that the off-site paper survey was not a “paper chase.”

One committee member asked if financial incentives could be given as a reward for good performance. Ms. Yost responded that currently there is a problem with the CLIA fees supporting the program costs. The member then suggested redistribution of the financial burden based on performance, which Ms. Yost agreed could be considered.

In general, the Committee agreed with the idea of providing laboratories incentive to reduce the inspection burden but believed laboratories should continue to be monitored and an initial onsite survey is needed as a baseline. Inspections should focus on outcomes and correlation with patient results, and the requirements should be less burdensome but not at the expense of the patient.

REVIEW OF THE IMPLEMENTATION OF PERSONNEL STANDARDS Addendum G

A review of the history of the development of the personnel standards in the current regulatory model was presented by Ms. Rhonda Whalen, Laboratory Practice Standards Branch. It was emphasized that the requirements are interrelated and are balanced to establish minimum standards of quality the laboratory must meet. The final regulations established personnel standards appropriate to ensure that low volume, limited service laboratories would be able to continue testing while large volume laboratories would be able to perform testing in a manner suitable for that environment. However, the Department has received a wide range of comments

that the personnel regulations are either too stringent and need to be revised to, for example, only require a qualified director who would be responsible for ensuring that laboratory personnel are qualified; or too lenient with respect to general supervisor, and the requirements should be revised to require, at a minimum, a bachelor's degree. At this point, the Committee was asked to comment on whether the personnel requirements are, in general, appropriate.

Committee Discussion

One committee member asked how it was possible to establish the minimum standards required to assure quality since there is limited data relating personnel qualifications to laboratory performance. Ms. Whalen responded that in formulating the regulations, consideration was given to public comments and input from consultants, but the variety of laboratories which would be regulated under CLIA made it difficult to set minimum standards. Access to care had to be considered and there was concern that if the qualification requirements were too high, they would be impossible to meet and access to laboratory services would be limited.

One committee member questioned the rationale for the discussion since the Committee previously had provided considerable input to the personnel qualifications and responsibilities. Dr. Baker explained that it would be helpful for the Committee to provide some general comment on the approach taken in establishing the personnel requirements, whether the approach was appropriate and if laboratories are having difficulty meeting the personnel requirements. The inspection data indicate that laboratories are in compliance so the assumption is that laboratories do not find the requirements difficult to meet.

A committee member stated that the supply and demand issues which existed two years ago are no longer applicable. In fact, the committee member noted that currently there is no shortage of medical technologists. However, one committee member commented that in rural and urban areas, public health laboratories have difficulty hiring qualified personnel to provide services to patients who are uninsured and complying with the CLIA responsibility requirements creates a hardship for directors of family planning clinics that have multiple laboratory sites. Another member stated that in rural areas the costs associated with employing medical technologists was an issue and that a person on-the-job trained was more desirable. A couple of committee members stressed the negative impact the regulations have had on baccalaureate education and training programs. Graduates of these programs can not find jobs, and schools have closed because the regulations only require high school graduates or individuals with an associate degree to perform testing. It was noted that lowering personnel standards results in people with minimum education performing laboratory testing, jobs in laboratory services are no longer attractive, and CLIA has played a role in this trend.

One committee member observed that competence is related to the environment and is situation-dependent and noted that the current personnel standards are totally inadequate and do not even provide a minimum standard for quality. She asserted that individuals who argue that standards are unnecessary make unfounded assumptions, such as, the existence of a host of safe guards in

the system that negates errors in laboratory testing. She was puzzled why there continues to be challenges to the need for standards in laboratory services when it is widely recognized that other health professionals (i.e., registered nurses and physicians) have standards of competence including education and certification requirements. The committee member noted that concerns about personnel qualifications are financial and are not related to quality. Another member agreed and stated that if financial resources were not involved, there would be no question about compromising quality. One member stated that for performance of any laboratory test, personnel need a basic knowledge of science and an understanding of what can go wrong during test performance, and that the goal should be to improve test quality but this goal cannot be achieved by continually lowering personnel standards to save money.

Another committee member stated that the focus needs to be on establishing the acceptable level of performance, whether it is at a single level or multilevel, and determining what is necessary to achieve that level of quality. He pointed out that there are laboratory activities that are simple, push button, and require no judgment, but others require training and experience to make good interpretations and decisions and these need to be identified. When testing requires higher levels of knowledge, this type of testing is easily recognized, the problem is how one would assess the level of knowledge required to operate an instrument. He also stated that if the personnel requirements are going to be reconsidered, one must build a structure that defines the need, specifies the demands or desired outcome, and defines the parameters or the bottom line that one is willing to accept; then the educational infrastructure must be established to meet this need.

Several committee members commented that the “grandfather” provisions were appropriate but noted that the general supervisor is the key to laboratory quality and the education requirement should be set prospectively to require, at a minimum, a baccalaureate degree in a science. One committee member noted that although the “grandfather” provisions have been added to the regulations, the Department had not acted on the CLIAC recommendations to require general supervisors in the future to have a baccalaureate degree; and in the committee member’s opinion, the current regulations allowing individuals with an associate degree plus two years training or experience to serve as general supervisor are appalling.

Committee opinion varied on the minimum qualifications required for testing personnel. Two committee members commented that the major problem is the law which requires site neutrality, resulting in a “one size fits all” regulation. Many committee members felt that there are problems with the complexity model and commented that both high and moderate complexity have too large a range of tests and that along with test complexity, laboratory function needs to be considered. Some committee members felt that the test complexity categories should be multi-tiered.

Dr. Collins asked how the Committee felt about maintaining the general supervisor and director requirements but allowing these individuals to choose the qualifications for testing personnel. There was limited discussion about this proposal; however, committee members agreed that it would be unwise to make any changes in the personnel requirements until longitudinal data on

laboratory personnel and performance are collected and analyzed.

CLIA REQUIREMENTS FOR QUALITY CONTROL

Addendum H

Dr. Tom Hearn began with the provisions in the law related to quality control (QC) and then presented background on how the QC requirements are balanced with other standards. The phase-in of the QC requirements applicable to moderate complexity commercial test systems and the minimum requirement of testing two levels of control every 24 hours were discussed. It was noted that the guiding principles used to establish the CLIA requirements included: QC is the process used to prevent and detect laboratory errors; the QC process must monitor environmental conditions, specimen manipulation and testing performance; and QC materials (samples) should meet the current National Committee for Clinical Laboratory Standards (NCCLS) definition. It was also noted that most errors occur outside the testing (analytical) process. In inspected laboratories, the most frequently cited deficiencies were related to the requirement to test two levels of control and failure to follow manufacturers instructions.

Committee Discussion

Two committee members asked for the rationale for the quality control phase-in. Dr. Hearn explained that the purpose of the phase-in was to allow previously unregulated laboratories time to become familiar with the QC requirements and to allow FDA sufficient time to develop a process to review manufacturers' QC instructions for compliance with CLIA QC requirements. The member then asked how the FDA would establish this process since the FDA has no resources for this purpose and questioned the reason for extending the phase-in when it appears that the FDA will not be reviewing manufacturers' QC instructions for CLIA compliance. Dr. Steve Gutman, of the FDA, responded that at this time the FDA has not established a review process for clearing manufacturers' instructions for CLIA compliance. He stated that the FDA continues to clear products under the 510(k) and premarket approval (PMA) processes.

Dr. Baker assured the Committee that the Department is aware of the problem and is looking at other strategies including clarifying what types of QC laboratories need to perform and recognizing the role of manufacturers in defining QC for devices.

The manufacturer liaison explained that FDA's 510(k) and PMA submission requirements require manufacturers to provide information pertaining to the test system's labeling instructions which include QC protocols. Prior to CLIA, the FDA's review of the test system's labeling included any QC procedures that the manufacturer believed to be appropriate to monitor the test system's performance. However, after CLIA implementation, the FDA has increased its scrutiny of manufacturers' QC statements and is ensuring that the QC instructions are clear and specify the portion of the test system monitored, and FDA does question QC instructions that are inconsistent with the CLIA requirements. The manufacturer liaison concluded by stating that for many products, the manufacturers' QC would be in conformance with the CLIA QC requirements, for other products, particularly new technology, many manufacturers feel that the

CLIA QC requirements are excessive. In this committee member's opinion, the QC phase-in extension was a disappointment to manufacturers because more flexibility needs to be added to the CLIA QC requirements to accommodate new technologies since some of these devices do not require six-month calibration or testing two controls each day of patient testing.

Dr. Gutman explained that under the Federal Food, Drug and Cosmetic Act, the FDA is concerned with performance standards of products, but the emphasis in the 510(k) clearance process is substantial equivalence to a predicate device (a product that has been cleared by the FDA). The FDA has always evaluated a device's precision and bias in relation to a reference method and in fact, the FDA may require that test system instructions include QC protocols that are more stringent than CLIA if it is felt that more than two controls are needed to monitor test system performance. While the FDA does not provide direction in terms of the frequency of testing QC materials, it does determine whether the manufacturer states in its instructions the portion of testing monitored by the control(s).

One committee member pointed out that the current QC standards were developed because unregulated laboratories were opposed to the QC requirements and as a result, the QC standards were "watered down" to accommodate site neutrality. The committee member noted that not all test systems categorized as moderate complexity are kits and in fact, the moderate complexity category includes many complex instruments such as Coulter™ counters that require sophisticated quality control and analysis. In this committee member's opinion, the list of moderate complexity tests is too diverse for the minimum QC requirements that are in effect during the phase-in, and the QC regulations are totally inadequate for the large sophisticated instruments categorized as moderate complexity.

A committee member asked about the difference between moderate and high complexity testing by suggesting that for moderate complexity tests, the burden is on the manufacturer to validate the method as opposed to the requirement for the laboratory to verify or establish the performance specifications for high complexity testing. CDC explained that during the phase-in, laboratories performing testing using commercially available, unmodified moderate complexity test systems are not required to perform a method validation. However, for all other testing, the performance specifications must be established or verified by the laboratory before testing patient specimens. Another committee member suggested that the CDC conduct a study that would compare performance between laboratories that validate test systems and laboratories that follow the minimum phase-in requirements and do not verify manufacturers' test system performance specifications. The manufacturer liaison stated that allowing the laboratory to verify the manufacturer's performance specifications in lieu of requiring laboratories to establish the test performance specifications was working well and suggested that CDC initiate a retrospective study to evaluate this process.

One committee member stated that the quality control requirements are minimal and with the variety of test systems available, the laboratory has the responsibility for determining which test methods are appropriate for the laboratory's test menu and, in addition, deciding on the best QC

practices to employ. The committee member suggested that instead of laboratories concentrating QC efforts on individual test systems, kits or devices, the focus should be on the laboratory's overall QC program.

CDC responded that when the QC requirements were developed, it was felt that QC should be required for all testing and there should be no difference between the QC requirements for moderate and high complexity. The QC phase-in was created to allow manufacturers time to develop their QC protocols for FDA CLIA clearance but ultimately after the phase-in the QC requirements would be the same for moderate and high complexity testing.

In reference to matrix problems, Dr. Schwartz asked if the QC materials were supposed to meet NCCLS guidelines and if there had been an effort to encourage manufacturers to meet the NCCLS standard. CDC responded that the intent was to have laboratories employ controls that are as close as reasonably possible to the type of patient specimens tested. This elicited discussion about the use of alternate control systems with some testing devices and new technology. CDC asked for Committee opinion about the use of internal, procedural, and electronic controls. Since many of these controls only monitor the analytical process, CDC asked how the Committee felt the rest of the testing process should be monitored as required by the regulations. While many committee members agreed that flexibility is needed for new technology, not all "controls" are true monitors of the total testing process and these materials can not substitute for quality control on some devices.

A committee member pointed out that the data presented earlier in the meeting indicated that the majority of testing errors occurred in the pre and postanalytic phases of testing and consequently to focus on the analytic phase is inappropriate and much too narrow. Monitoring the pre and postanalytic phases have to be included in the laboratory's QC of the test system.

A committee member stated that the CLIA regulations include requirements for quality assurance (QA) which address the pre and postanalytic phases of testing; however, he thought QA was not included in the proposed APT subcategory. The committee member suggested using the term total quality process instead of quality assurance. Another committee member agreed that quality control on an APT instrument should be part of the laboratory's quality control monitoring process. Dr. Collins responded by emphasizing that the proposed APT subcategory includes requirements to monitor the total testing process i.e., QA, QC, and PT.

A few members stated that some previously unregulated laboratories did not know how to meet the QA requirements which are too vague and allow too much flexibility leading to misinterpretation, and these members indicated that more specific guidance is needed to assist laboratories in meeting the QA requirements.

Returning to the QC discussion, Ms. Yost emphasized the dilemma for surveyors in evaluating laboratories that use procedural controls to monitor testing. Based on the Committee discussion, the total testing process needs to be monitored by testing QC. However, she pointed out that for

commercially available, unmodified moderate complexity testing, during the QC phase-in, surveyors have been allowing laboratories to meet the QC requirements by performing whatever QC the manufacturer recommends for the test system. These controls often only verify the viability of reagents but do not monitor the total testing process. She asked the Committee for input on whether this practice should continue or whether the entire testing process as defined by NCCLS, should be monitored and should there be a difference between the QC requirements for moderate and high complexity testing.

A committee member pointed out that the electronic checks for some devices monitor the process of the instrument converting a sample signal to an electronic signal, however, this check does not monitor the entire process. He added that the process of specimen extraction should be evaluated but this varies by instrument or is system dependent. Ms. Yost agreed and pointed out that testing could be affected by temperature, humidity, reagent expiration, etc., and if the control(s) do not evaluate the whole testing process, there is no way of detecting problems with these factors. These undetected problems could result in inaccurate test values regardless of the electronic control checks.

One committee member suggested that the financial implications should be considered and cited the example of single test unit strep tests in which testing a positive and negative control requires separate test units. He also added that the detection of group A streptococcus is dependent on proper specimen collection and questioned how one would monitor this testing phase.

Another committee member replied that quality control for specimen collection is included under quality assurance which requires laboratories to have a mechanism to monitor the total process, including the pre and postanalytic phases of testing. She added that surveyor training needs to include how to evaluate each instrument and determine whether appropriate control mechanisms are in place.

Another committee member stated that the focus should be on determining what part of the testing process is not being monitored and the error detection rate of procedural or component controls versus testing two levels of control that monitor all phases of testing. He noted that this information should be provided before the Committee recommends changing any of the CLIA QC requirements. This was seconded by the Committee chairman.

The Committee chairman stated that these quality control issues should be examined more closely at another CLIAC meeting either by the full Committee or the QC subcommittee. He suggested that QC requirements for new technology be a topic for a future meeting and requested that scientific data pertaining to test system accuracy when testing is performed in accordance with manufacturer's instructions be presented. Dr. Collins agreed that it was appropriate to get advice from CLIAC on QC issues and again reminded everyone of the upcoming institute "Frontiers in Laboratory Practice Research" in which these topics would be discussed.

COMMITTEE BUSINESS/PUBLIC COMMENTS

Presentation of Plaques for Outgoing CLIAC Members

Dr. Schwartz made the announcement that a few members of the CLIAC were ending their terms of service and presented the following members with individual plaques commemorating their service: Dr. Paul Bachner, Ms. Virginia Charles, Dr. Stanley Inhorn, and Dr. Kenneth Matthews.

Public Comments

Mr. Robert J. Slomoff, representing HemoCue, expressed concern regarding the policy on granting automatic waived status to products cleared by the FDA for home use. Mr. Slomoff noted that the focus of the review for waived categorization is quite different from the FDA clearance process. FDA clearance for home-use is for home-use and these products are not intended for use in a laboratory. He then stated that if FDA home use clearance means that a test is waived under CLIA, then CDC and FDA should harmonize their requirements and have similar standards.

Dr. Schwartz noted the Committee's concern that FDA clearance for home use results in automatic waiver status. Dr. Gutman responded that the FDA is willing to consider changes to the FDA review process. He agreed that the FDA process is more of a "truth in labeling" process which is different from the CDC review process for waiver. FDA's focus has been to determine whether performance of a device is equivalent to a device that has been cleared. The review process for home use has been more contingent on the public health need and usefulness of the device and not so much related to scientific justification. FDA does not look at random or systemic error but whether total error matches intended use, whereas CDC looks more at the statistics related to laboratory test performance. FDA would be willing to work with the CDC to harmonize the processes but the outcome may be more strict or less strict and might not necessarily satisfy the Committee.

Observing the incompatibility between the FDA home use clearance process and the waiver review process, which includes the determination that there is an insignificant risk of erroneous result for waived tests, a committee member expressed concern about the policy to waive test systems cleared by the FDA for home use. Another committee member pointed out that in the FDA review, public health is a concern for home use clearance, but if these home use test systems are waived, it could be a public health crisis since these devices could be used in intensive care units throughout the country, and waived tests are not subject to personnel or quality control standards. She noted that the criteria for waiver must be as stringent as possible. She also stated that those devices that are currently waived should be retrospectively evaluated.

Another committee member pointed out that although the FDA has very thorough labeling requirements for home use devices and more latitude in the guidelines for clearance of these devices, the guidelines used to clear devices for use in laboratories should be more stringent because of potential errors and their impact.

Ms. Polly Cathcart, representing the American Society of Clinical Pathologists, expressed general concern that the I-Stat device was under review for waiver and referenced specific areas of concern using the CDC guidelines for test characteristics, storage, and accuracy.

One committee member stated that the examples of problems described in testing using the I-Stat instrument are things a manufacturer's study may not show but could be seen in the laboratory. Another member inquired how the public could find out which devices or test systems are under review for waiver. Dr. Collins responded that the manufacturer may make the application public, but the CDC kept the applications confidential. Dr. Schwartz stated that the CLIAC may need to get involved in the review of multianalyte instruments. Dr. Collins also stated that any tests granted waiver are published as a notice in the Federal Register which provides an opportunity for public comment. A committee member pointed out that if the test was approved for waiver, and then published in a Federal Register notice with a comment period, the device could be in use for a long period of time before the comments are analyzed and any necessary changes are made.

Toni Casey, a representative of I-Stat, responded that information on the precision and accuracy of the I-Stat would be provided to the members.

One committee member stated that manufacturers were obligated to follow-up on complaints about devices and if there are publications indicating inaccuracy, the manufacturer has to investigate the claim and take action or notify the users of the device limitations. Another member reiterated that the FDA and CDC review processes should be aligned and suggested that one or both agencies report at the next meeting on how close the two processes are in reaching alignment.

John Bruni, representing Biosite Diagnostics, commented that the waiver process should take into consideration the intended use of the product and each individual product should be evaluated according to intended use and not use guidelines that broadly apply to all devices.

David Phillips, representing Boehringer Mannheim Corporation, commented that some devices are unitized, and that procedural and electronic controls should be acceptable QC for those test systems. He noted that QC can be performed on a cartridge but the patient sample would be tested with another cartridge. He gave the example of testing IV solutions for sterility by lot number and stated the same principles could be applied to point-of-care instruments since the manufacturer produces cartridges, strips, etc., in lot numbers. Dr. Schwartz asked what failure rate is acceptable to the manufacturer. Mr. Phillips responded that there should be a 95% confidence interval and recommended that laboratories perform a random check from each

shipment and lot number to verify acceptable limits.

One committee member agreed but questioned how this would be different from instruments used in non-point-of-care sites. Another committee member stated that there was no difference and that the issue was not about validating individual cartridges but looking at the entire testing process. If each step in the testing process is identified, then you can evaluate which parts of the test system need to be monitored based on the conditions that affect testing.

A committee member stated that in order to determine failure rate, he thought failure would need to be defined. There is a cost issue when dealing with unitized devices and suggested that when a shipment of reagents arrives in the laboratory, a full scale QC should be performed. After this initial check, he thought that the shipment of reagents should be reliable and further QC of the test system should not be necessary. However, he noted under CLIA, QC is required each day patients are tested.

Conflict of Interest

Each committee member disclosed his/her financial interest(s) relevant to the topics discussed during the meeting.

Summary

In closing, Dr. Baker summarized the Committee's suggestions and briefly outlined possible topics for future CLIAC meetings:

- The Committee should be provided an opportunity to discuss the comments received to the APT proposed rule before publication of the final rule.
- CDC should ensure that reviews of waiver requests are consistent and accurate and at CDC's request, CLIAC would review any proposed clarifications to the statutory criteria for waiver, provide oversight in the implementation process and evaluate application of the waiver guidelines to a specific device;
- The CDC and FDA should work towards achieving greater congruence between CDC's review process for waiver and FDA's home use clearance process;
- CLIAC should play an advisory role in reviewing the QC regulations and any revisions to the CLIA QC requirements as they apply to new technology and could consider the issue of test specific QC requirements versus requirements for an overall laboratory QC program;
- CLIAC may examine and discuss the effects, if any, of managed care on laboratory services;

- CLIAC supports deferring any recommendations for revisions to the personnel qualification requirements until data on laboratory personnel and performance are collected and analyzed; and
- Information pertaining to current genetics testing practices should be presented to the CLIAC to determine what recommendations, if any, the Committee should make in this area of laboratory testing.

Future Meetings

Dr. Schwartz asked that the committee members consider dates for the next two CLIAC meetings. The members agreed to schedule full committee meetings on August 30-31, 1995 and January 24-25, 1996.

I certify that this summary report of the May 10-11, 1995 meeting of the Clinical Laboratory Improvement Advisory Committee is an accurate and correct representation of the meeting.

/S/ Morton K. Schwartz, Ph.D.
Chairman